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Mini Review

Chromatin diminution and its possible biological meaning

Abyt Ibraimov*

International Higher School of Medicine, Bishkek, Kyrgyzstan.

***Corresponding Author:** Abyt Ibraimov, International Higher School of Medicine, Bishkek, Kyrgyzstan.

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Abstract:

Chromatin diminution (CD) is a phenomenon of germline and somatic cell differentiation during early embryonic development, associated with the loss of a portion of chromatin that represents the chromosomal constitutive heterochromatin (CH). In CD, 96-98% of chromatin is deleted in somatic cells (macronucleus), whereas in germline cells (micronucleus) they are completely preserved. Despite the fact that the phenomenon of CD was discovered in the in the late 18th century, its biological role remains to be elucidated. Numerous hypotheses have been proposed, which are the subject of discussions. Based on data obtained during the study of variability of human CH, the hypothesis of their participation in cell thermoregulation (CT) was substantiated. The essence of CT is that it equalizes temperature differences between the nucleus and cytoplasm, namely, excess metabolic heat from the cell nucleus is removed into the cytoplasm by means of a dense layer of condensed chromatin (CC) around the nucleus, consisting of CH. We discuss the view that the phenomenon of CD in parasitic animals may be related to CT in somatic cells, in the sense that in them the problem of thermoregulation is solved by the host organism and for this reason they do not need to retain full CH as the material basis of CT. Chromatin preservation in germ cells is necessary for conjugation, synaptonemal complex formation and recombination of homologous chromosomes during meiosis.

Key words: chromatin diminution; constitutive heterochromatin; cell thermoregulation; condensed chromatin

Introduction

Theodore Boveri [1887] first discovered the phenomenon of chromatin diminution. Chromatin diminution is a general name for cellular processes during which, in the early embryonic development of some multicellular animals, cells lose part of chromatin material, which are chromosomal constitutive heterochromatin, in a programmed manner. In chromatin diminution, 96-98% of constitutive heterochromatin is deleted in somatic cells (macronucleus), whereas in germline cells (micronucleus) they are completely preserved. In the somatic cell line, the remaining DNA of the genome is sufficient to perform all necessary functions of an adult organism. The eliminated DNA can undoubtedly be considered as non-coding DNA for somatic cells, since the absence of this part of the genome in them does not interfere with the normal course of ontogenetic processes.

Chromatin diminution is observed in 12 species of parasitic nematodes and is not found in free-living nematodes. It is also observed in some species of ascarids, cyclops, infusoria, mites, beetles, butterflies, flies and fish. The mechanisms of diminution differ in different organisms, but what unites them is that mainly repetitive and non-coding DNA is lost, and this occurs only in somatic tissue embryos.

Despite the fact that the phenomenon of chromatin diminution has been studied for over a hundred years, its biological role remains to be elucidated. There is an extensive literature on this topic and it is beyond our scope to analyze them. In particular, it is proposed to consider chromatin diminution as a universal mechanism of genome reduction, reducing the frequency of recombination events in the genome, which leads to specialization and adaptation of the species to more narrow environmental conditions. The most complete list of existing hypotheses about the biological significance of programmed DNA elimination (chromatin diminution) suggests the following functions: gene silencing and regulation, nucleotypic effects, mutation rate reduction, and energetic benefits (Grishanin 2014; 2024; Wang and Davis 2014; Dedukh and Krasikova 2021; Drotos et al. 2022; Kloc et al. 2022).

It seems to us highly probable that the biological meaning of removing a significant part of chromosomal constitutive chromatin in somatic cell lines is related to the problem of thermoregulation. As is known, all

multicellular organisms strive to maintain a relatively constant temperature in the body (temperature homeostasis) necessary for the fulfilment of their normal life activity. For this purpose, they use all available means, including the production of additional heat energy through cellular metabolism, to maintain a positive body temperature.

As is known, the main source of heat energy in the organism is cellular metabolism, accompanied by the release of heat, including excess heat, which must be timely removed outside the cell. In this process in the most difficult position is the cell nucleus, the temperature of which, as a rule, is higher than in the cytoplasm. In order to remove excessive heat, the nucleus has two options at its disposal: to increase its volume or to find a means contributing to the effective removal (dissipation) of heat energy into the cytoplasm. Since the first option is excluded for known physical reasons, the second option remains, to increase the thermal conductivity of the nuclear envelope. However, as it is known cell membranes by their nature cannot be reliable heat conductors, because their physical integrity and useful biological properties are strongly affected by temperature fluctuations above or below the physiological optimum for a given species. Perhaps for this reason Nature invented a simple remedy: to use the layer of condensed chromatin around the nucleus, which is the densest structure in the interphase cell, as a suitable heat conductor.

Thermoregulation at organism level is the well-established fact. The question on possibility of thermoregulation at the cell level remains opened. Based on study of distribution of chromosomal constitutive heterochromatin regions in the genome of various human populations, in norm and at some forms of pathology the hypothesis about thermoregulation existence at the cell level has been presented. The essence of hypothesis of cell thermoregulation is elimination of the temperature difference between the nucleus and cytoplasm when the nucleus temperature becomes higher than in the cytoplasm. The nucleus, in contrast to the cytoplasm, cannot conduct heat directly in the extracellular space, from where the heat is taken by the circulating flow of blood and lymph. Thus, the nucleus can transfer surplus heat only in the cytoplasm. With this, the nucleus has two options: either by increasing its volume or increasing the heat conductivity of the nuclear envelope. As the first option is limited, and the second one is hampered because of tenderness of the cell membranes, apparently the higher eukaryotes took advantage of the opportunity of a dense layer of peripheral condensed chromatin as heat conductor for a more efficient elimination of the temperature difference between the nucleus and cytoplasm. The condensed chromatin localized between a nucleus and cytoplasm is made of chromosomal constitutive heterochromatin, which are one of the forms of higher organization of non-coding, so-called "excess" DNA in the genome of higher eukaryotes. The biological role of “excess DNA” in eukaryotes, which consists of short repeating sequences of nucleotides and does not code for proteins and enzymes remains unclear. The part of this DNA in the interphase cell is complexed with proteins into highly compacted structures, referred to as condensed chromatin. The biological role of non-coding DNA, which form a dense layer of condensed chromatin around the cell nucleus in the interphase cell, is their participation in maintaining intracellular temperature homeostasis [Ibraimov 2003; 2004, 2019; 2020; 2023].

As is known, the main source of heat energy for all organisms is cellular metabolism. This source of energy is used primarily to maintain normal life activity of a given organism. However, multicellular organisms, in order to maintain temperature homeostasis in the body, need to generate additional heat energy by increasing the load on cellular metabolism. This process, unfortunately, is accompanied by the production of excess heat energy, which is not used by organisms to perform useful biological work and need their timely removal outside the cell. From our point of view, it is for this purpose that the mechanisms of cell thermoregulation exist. In this sense, parasitic worms are exceptions in the sense that they do not need to produce additional heat energy to maintain temperature homeostasis in the body, because this task is undertaken by the host organism itself, by creating a relatively constant temperature in the environment.

If our reasoning is correct, then it is not difficult to imagine that, for example, parasitic worms living in the human small intestine do not need to preserve chromatin in full for the following reasons: 1) preservation of chromatin in ontogenesis requires a lot of energy and material resources, which is not always easy; 2) the optimal ambient temperature for parasite activity is provided by the host itself; 3) there is no need for worms to generate additional thermal energy to maintain body heat, which is not possible without the participation of cell thermoregulation and constitutive heterochromatin.

In other words, the biological meaning of the phenomenon of chromatin diminution can be explained from energetic considerations. Firstly, preservation of chromatin in full volume in all cells throughout ontogenesis is both energetically and materially unnecessary, if in individual development it is possible to do without their participation. Secondly, chromosomal constitutive heterochromatin being the main component of cell thermoregulation is especially important when the organism needs to constantly produce additional heat energy to maintain temperature homeostasis in the body. And chromatin in germ cells is preserved because it is necessary for conjugation, synaptonemal complex formation and recombination of homologous chromosomes during meiosis without which adaptation and evolution are impossible.

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